

**REMARKS**

Claim 19 has been added based on the disclosure at page 11, lines 7-8 in the present application. It is submitted that claim 19 is directed to elected subject matter.

Entry of the above amendment is respectfully requested.

**Request for Personal Interview with Examiner**

Applicants respectfully request a personal interview between the Examiner and Applicants' representative at a mutually convenient time prior to the Examiner acting on this application again.

**Obviousness Rejections**

On page 3 of the Office Action of February 2, 2010, claims 4-9 and 11-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimomura et al. (JP-2001-157574) in view of Johnsson et al. (Biophysical Journal 2001 80:313-323), Nishikawa et al. (Materials Research Society Symposium Proceedings 2002 724:N11.7.1-N11.7.6), and Maruyama et al. (Thin Solid Films 1998 327-329:854-856). Also, on page 5 of the February 2, 2010 Office Action, claims 4 and 9-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shimomura et al. in view of Huang et al. (U.S. Patent No. 5,283,122), Nishikawa et al., and Maruyama et al.

Applicants respectfully submit that the present invention is not obvious over the cited art combinations, and request that the Examiner reconsider and withdraw these rejections in view of the following remarks.

**1. Description of Johnsson / Huang**

According to the Advisory Action dated June 24, 2010, the Examiner still depends on Johnsson or Huang for negating unobviousness of the present invention in combination with Maruyama et al. However, Applicants submit that there are several misunderstandings about the description of Johnsson / Huang with regard to the following points.

a) The hexagonal structure of DOPE (Dioleoylphosphatidylethanolamine) in water is different from that in the present invention

According to the Examiner's understanding, DOPE in water forms a stable hexagonal structure since it is a water-insoluble amphiphilic molecule. However, the actual structure is a cylindrical one with infinite length, though its cross-section is circular and similar to the hexagonal structure of the present invention. In this regard, Applicants refer the Examiner to Figure 3 on page 3 of the attached Reference Material 1 (PMC Biophysics article). Also, Applicants refer the Examiner to the attached PowerPoint Fig. 1, which is based on Figure 3 of Reference Material 1).

On the other hand, the honeycomb structure of the present invention is formed by fine spherical droplets of water as a template. Though it can be seen as hexagonal from the above, it has a spherical void internally. The honeycomb structure of the present invention is not an array of hexagonal cylinders, but rather it has interconnected spherical voids internally. A void in the film is connected to adjacent six voids to form interconnected voids, which is a completely different structure from that in Johnsson or Huang. In this regard, Applicants refer the Examiner to the attached PowerPoint Fig. 2.

As a consequence, an ordinary artisan knowing the difference of the structures would not have utilized the teachings of Johnsson or Huang, i.e., a cylindrical structure, to prepare the honeycomb structure of the present invention.

b) The size is greatly different

In addition of the difference in shape mentioned above, the size is greatly different as well. Whereas the diameter of the hexagonal cylinder in Figure 3 of Reference Material 1 showing DOPE in water is 7.34 nm (see PowerPoint Fig. 1; the diameter is calculated based on the values given in section 2.3 of Reference Material 1, i.e.,  $2 \times 15.9 \text{ \AA} + 2 \times 20.8 \text{ \AA}$ ), the diameter in PowerPoint Fig. 2, i.e., the present invention, is about 5  $\mu\text{m}$ . Namely, the difference is about 1000 times. This indicates that the formation of the hexagonal structure described in Johnsson / Huang is a completely different physical phenomenon from the formation of the honeycomb structure in the present invention.

c) DOPE does not form a hexagonal structure in organic solvents

It was common technical knowledge that the hexagonal structure in Johnsson / Huang can only be found in water, so it could not have expected for an ordinary artisan to prepare the hexagonal structure in organic solvent.

d) A honeycomb film could not be prepared by using cholesterol, an amphiphilic molecule

If the Examiner were correct in that any amphiphilic molecule can be used to form the honeycomb structure of the present invention or Maruyama et al., it is deduced that one can

prepare a honeycomb structure by using cholesterol, an amphiphilic molecule. See page 559 of the attached Reference Material 2 ("Intermolecular and Surface Forces").

However, according to Applicants' experiment shown below, a honeycomb structure of the present invention cannot be prepared by using cholesterol as an amphiphilic molecule. This means the Examiner's inference that the honeycomb structure can be prepared by utilizing any amphiphilic molecule is incorrect.

[Experiment 1]

A chloroform solution of polylactic acid (molecular weight: 100,000) (5 g/L) was mixed with cholesterol as a surfactant in a ratio of 10:1. The mixture was cast on a glass plate and allowed to stand under a condition at room temperature and at a humidity of 70%. The solvent was gradually evaporated off for preparing a honeycomb structure. Namely, the preparation condition was completely identical to the examples of the present description except for the amphiphilic molecule used.

However, the resultant film did not have a honeycomb structure. The attached PowerPoint Fig. 3 is an optical photomicrogram of the film.

[Experiment 2]

A chloroform solution of polylactic acid (molecular weight: 100,000) (5 g/L) was mixed with cholesterol as a surfactant in a ratio of 200:1. The mixture was cast on a glass plate and allowed to stand under a condition at room temperature and at a humidity of 70%. The solvent was gradually evaporated off for preparing a honeycomb structure.

However, the resultant film did not have a honeycomb structure. The attached PowerPoint Fig. 4 is an optical photomicrogram of the film.

## **2. Misunderstanding of Maruyama**

The Examiner mentioned “Maruyama et al. teach that self-assembling molecules that form three-dimensional nanoscale structures are combined with polymers to form microscale features in structured films” in the final Office action dated February 2, 2010 (see page 4, lines 19-21; emphasis added). Based on this position, it seems that the Examiner deduced that nanoscale phenomena could be extended to microscale events. However, Applicants submit that this comprehension of Maruyama is incorrect.

“Introduction” on page 854 of Maruyama clearly distinguishes nanoscale events and microscale ones. The former relates to short-range forces acting on a molecular level such as Van der Waals force and Coulomb force in molecular assemblies. “On the other hand” (line 15), the latter relates to forces that act on a larger length-scale such as surface tension and convection. And formation of a honeycomb structure, which is microscale phenomenon, follows after this explanation. In any event, Maruyama never indicates that self-assembling molecules that form nanoscale structures are combined with polymers to form microscale features in structured films.

In addition, Applicants would like to focus on the word “combine” in this Examiner’s statement. Here, Applicants understand that the word “combine” does not mean formation of a covalent bond between the self-assembling molecules and the polymers. If it does, Applicants submit that Maruyama is completely irrelevant, since there is no covalent bonding between the biodegradable polymer and phospholipid in the present invention. Therefore, Applicants understand that “combine” means just blending of the self-assembling molecules and the polymers hereinafter. Even so, Maruyama does not provide any teachings in regard to this meaning, since the illustrated examples in Maruyama such as polyion complex or poly (styrene)-

poly (paraphenylene) block copolymers are not mixtures of self-assembling molecules and polymers but polymers themselves.

**3. An ordinary artisan would not have used a low molecular weight compound**

One of the references cited by the Examiner; Shimomura et al. (JP-2001-157574), whose whole English translation is attached as Reference Material 3, indicates in paragraphs [0004]-[0005] that even if amphiphilic polymers are used for preparation of honeycomb films, the resulting polymers “involve such problems as poor self-reliance of the honey-comb structure obtained, or chronological delay of the honey-comb structure, and have failed to provide a sufficient function as the substrate for cell incubation”. See paragraph [0005]. Under the circumstances, Shimomura solved this problem, i.e., insufficient self-support of the resulting film, by adopting a new amphiphilic polymer.

Knowing this technical problem, an ordinary artisan skilled in the art would not have used a low molecular weight amphiphilic compound instead of a amphiphilic polymer.

Thus, Applicants submit that the present invention is not obvious over the cited art, and withdrawal of these rejections is respectfully requested.

**Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

AMENDMENT UNDER 37 C.F.R. § 1.114(c)  
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Respectfully submitted,



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